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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/569,224	01/29/2007	Alasdair Craig Stamps	1300-1-013PCT/US	7472

23565 7590 03/06/2008

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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
03/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/569,224	STAMPS, ALASDAIR CRAIG	
	Examiner	Art Unit	
	MEERA NATARAJAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-26* is/are pending in the application.

4a) Of the above claim(s) *10,11 and 13-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/13/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 7-9 and 12 in the reply filed on 12/17/2007 is acknowledged.

2. Claims 10, 11, and 13-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/17/2007.

3. Claims 7-9 and 12 will be examined on the merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 7-9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 7 recites "an agent which interacts with or modulates the expression or activity of a KIAA0659 polypeptide". It is unclear what is meant by "interacts" and "modulates". The specification does not provide a definition for the terms in order to define the metes and bounds of the claim. Does applicant mean, binds to, belongs to a signaling cascade, inhibits expression or activity, enhances expression or activity, etc. Clarification is required.

7. Claim 12 recites "which retains the activity of the KIAA0659 polypeptide". It is unclear what is meant by "activity". Does it mean biological activity, binding properties, apoptotic activity, enzymatic activity, etc.? Clarification is required. Applicant is invited to consider amending the claims to recite the particular characteristics of "activity" intended by setting forth testable functions, provided there is written description in the specification as-filed.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C § 112, paragraph 1 "Written Description" requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in

possession of the genus (Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January, 2001, See especially page 1106 3rd column).

11. Regarding the instant claim limitations, the specification does not appear to provide an adequate written description for a "a derivative having one or more amino acid substitutions, modifications, deletions or insertions relative to the amino acid sequence of SEQ ID NO:1 which retains the activity of the KIAA0659 polypeptide". The present claim reads on any variant of SEQ ID NO:1 that "retains the activity of the KIAA0659 polypeptide". However, as stated in the 112 2nd paragraph rejection set forth above, the specification does not provide a definition for the term "activity". Therefore, one of ordinary skill in the art at the time the application was filed, would not have adequate guidance to identify variants of SEQ ID NO:1 which "retains the activity of the KIAA0659 polypeptide". Applicant fails to provide any identifying characteristics, physical or chemical properties, or a correlation between function and structure of the derivatives claimed. Applicants only provide disclosure for SEQ ID NO: 1 and do not provide support for derivatives of SEQ ID NO:1 comprising one or more amino acid substitutions, modifications, deletions or insertions of SEQ ID NO:1. They only describe SEQ ID NO:1. Therefore, the specification does not provide for sufficient written description to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, Applicant had possession of all derivatives of SEQ ID NO:1, which retains the activity of the KIAA0659 polypeptide.

12. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398.

13. Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

14. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

15. Claims 7-9 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

16. The claims are drawn to a method for the treatment and/or prophylaxis of *ANY* carcinoma comprising administering a therapeutically effective amount of an antibody which interacts with or modulates the expression or activity of a KIAA0659 polypeptide,

comprising SEQ ID NO:1 or a derivative thereof comprising amino acid substitutions, modifications, deletions, or insertions relative to the amino acid sequence of SEQ ID NO:1 which retains the activity of the KIAA0659 polypeptide.

17. The specification does not provide any teachings of the prophylaxis of cancer, how to determine the individuals who will develop a particular cancer, nor how to effectively prevent said particular cancer type before occurrence. Thus, one of skill in the art would not be able to use the composition of the invention as a vaccine without undertaking to determine how to select for individuals who will develop a particular cancer type before the said cancer occurs in the individual. An effective therapeutic protocol for the treatment or prevention of the formation of a tumor is subject to a number of factors, which enter the picture beyond simply the administration of the claimed composition.

18. The art teaches the unpredictability of antibody-based cancer immunotherapy. Christiansen et al (Mol Cancer Ther, 2004, 3:1493-1501) teach numerous factors that inhibit successful therapeutic application of antibodies including low or heterogeneous expression of target antigens by tumor cells, high background expression of target antigen on normal cells, host antibody immune responses to the antibodies themselves, insufficient antitumor response after antibody binding, as well as significant physical barriers preventing antibody binding or delivery to a solid tumor mass, including the vascular endothelium, stromal barriers, high interstitial pressure, and epithelial barriers (abstract; p. 1493, col. 2; p. 1496, col. 1, last paragraph through p. 1498, col. 2). Topp et al (Journal of Controlled Release, 1998, 53:15-23) teach the complications and

unpredictability involved with treating tumors using immunoconjugate therapy. Topp et al teach that immunoconjugates are composed of an antibody or fragment thereof linked to a drug, toxin, or radioisotope. Topp et al teach that there are several barriers to successful delivery of immunoconjugates to extravascular sites of action within target tissues: the immunoconjugates must be absorbed into the blood stream, carried by the circulatory system to the capillaries in the target tissue, cross the capillary endothelial cells and the underlying basement membrane that supports the capillary structure and penetrate through the matrix of cells and extracellular components that comprises the tissue itself, bind to the cell surface receptor, initiate endocytosis, encounter possible drug degradation and drug release. Additional connective tissue barriers may also be encountered (p. 15, both columns; Figure 1). While immunoconjugates have been shown to be effective *in vitro* the results of clinical trials have been disappointing. The inability of the immunoconjugate to penetrate the tumor mass could be a cause of this lack of clinical efficacy. Topp et al cautions against extrapolating *in vitro* results to *in vivo* therapy stating that the cell culture system has some limitations including a lack of well-developed extracellular matrix ("stroma") that is present in many tumors. Normal components of tumor stroma include collagen, fibronectin and glycosaminoglycans (p. 21, col. 2).

19. In view of the contemporary knowledge in the art of the general lack of successful application of monoclonal antibody-based therapy methods for the treatment of human diseases and of the limited predictive value of in vitro results for efficacy in

human, those of skill in the art would not view applicant's assertions that the composition comprising a KIAA0659 antibody is useful for treating human cancers.

20. In addition the claims are broadly drawn to a method for the treatment and/or prophylaxis of carcinoma comprising administering a KIAA0659 polypeptide or a derivative comprising amino acid substitutions, modifications, deletions, or insertions relative to the amino acid sequence of SEQ ID NO:1. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

21. Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a super agonist with 5 times the activity of nature human insulin (Schwartz et al, Proc Natl Acad Sci 1987). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase (Lin et al Biochemistry 1975).

22. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. The results of the construction of synthetic proteins

remain very unpredictable as Burgess et al, Lazar et al, Schwartz et al, Lin et al conclusively demonstrate. Undue experimentation would be required in order to determine which specific amino acids of SEQ ID NO:1 could be substituted, modified, or deleted and still retain the activity of the KIAA0659 polypeptide. The specification provides no guidance for determining these derivatives of SEQ ID NO: 1.

Claim Rejections - 35 USC § 102

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. Claims 7-9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al. (WO/2001/066689).

25. The claims are drawn to a method for the treatment of a carcinoma comprising administering a therapeutically effective amount of an antibody which interacts with or modulates the expression or activity of a KIAA0659 polypeptide, comprising SEQ ID NO:1 or a derivative thereof.

26. Tang et al teach methods for the treatment of cancer comprising administering to a subject a therapeutically effective amount of a composition comprising an antibody that binds to the KIAA0659 polypeptide (see pg 4, lines 29-32 and pgs. 52-54). Tang et al. teach SEQ ID NO: 340, which is identical to SEQ ID NO:1 of the instant application. Tang et al. teach monoclonal, polyclonal, chimeric, humanized, and conjugated antibodies to a detectable label, cytotoxic agent or cytokine (see pgs. 74-84) that

specifically bind to the KIAA0659 polypeptide (see pgs. 74-84). The reference therefore anticipates the claimed invention.

Conclusion

27. Claims 7-9 and 12 are rejected.

28. No claim is allowed.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is (571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

/Larry R. Helms/
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